# WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Thursday, February 24, 2005

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
| | | *DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR* | |
| ☐ | L13 | (vary or varying) with size with linker | 63 |
| ☐ | L12 | library same (vary or varying) with size with linker | 8 |
| ☐ | L11 | library same (vary or varying) with length with linker | 54 |
| ☐ | L10 | L9 not l7 | 0 |
| ☐ | L9 | random same (vary or varying) with length with linker | 13 |
| ☐ | L8 | L7 not l5 | 0 |
| ☐ | L7 | random same (vary or varying) with length with linker | 13 |
| | | *DB=PGPB,USPT; PLUR=YES; OP=OR* | |
| ☐ | L6 | triplet same (vary or varying) with length with linker | 0 |
| ☐ | L5 | random same (vary or varying) with length with linker | 13 |
| ☐ | L4 | (vary or varying) with length with linker | 555 |
| ☐ | L3 | (vary or varying) with length and L2 | 1 |
| ☐ | L2 | random and L1 | 1 |
| ☐ | L1 | 5837242.pn. | 1 |

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1639MLS

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| | | | |
|---|---|---|---|
| NEWS | 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS | 2 | | "Ask CAS" for self-help around the clock |
| NEWS | 3 | SEP 01 | New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! |
| NEWS | 4 | OCT 28 | KOREAPAT now available on STN |
| NEWS | 5 | NOV 30 | PHAR reloaded with additional data |
| NEWS | 6 | DEC 01 | LISA now available on STN |
| NEWS | 7 | DEC 09 | 12 databases to be removed from STN on December 31, 2004 |
| NEWS | 8 | DEC 15 | MEDLINE update schedule for December 2004 |
| NEWS | 9 | DEC 17 | ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 10 | DEC 17 | COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 11 | DEC 17 | SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 12 | DEC 17 | CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected |
| NEWS | 13 | DEC 17 | THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB |
| NEWS | 14 | DEC 30 | EPFULL: New patent full text database to be available on STN |
| NEWS | 15 | DEC 30 | CAPLUS - PATENT COVERAGE EXPANDED |
| NEWS | 16 | JAN 03 | No connect-hour charges in EPFULL during January and February 2005 |
| NEWS | 17 | JAN 26 | CA/CAPLUS - Expanded patent coverage to include the Russian Agency for Patents and Trademarks (ROSPATENT) |
| NEWS | 18 | FEB 10 | STN Patent Forums to be held in March 2005 |
| NEWS | 19 | FEB 16 | STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005 |

NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

| | |
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| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS INTER | General Internet Information |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS PHONE | Direct Dial and Telecommunication Network Access to STN |
| NEWS WWW | CAS World Wide Web Site (general information) |

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                  * * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:53:52 ON 24 FEB 2005

=> (vary or varying) (10A) (size or length) (10A) linker
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> fil medline biosis caplus embase wpids
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.63       0.63

FILE 'MEDLINE' ENTERED AT 12:55:38 ON 24 FEB 2005

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FILE 'WPIDS' ENTERED AT 12:55:38 ON 24 FEB 2005
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=> (vary or varying) (10A) (size or length) (10A) linker
L1            87 (VARY OR VARYING) (10A) (SIZE OR LENGTH) (10A) LINKER

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2            39 DUP REM L1 (48 DUPLICATES REMOVED)

=> library and l2
L3             7 LIBRARY AND L2

=> t ti l3 1-7

L3   ANSWER 1 OF 7      MEDLINE on STN
TI   Optimizing the stability of single-chain proteins by linker length and
     composition mutagenesis.

L3   ANSWER 2 OF 7  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Genetic analysis of the nsP3 region of Sindbis virus: Evidence for roles
     in minus-strand and subgenomic RNA synthesis.

L3   ANSWER 3 OF 7  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
TI   Novel polypeptide antigen which includes epitope overexpressed by tumor
     cells e.g. B-cell lymphoma, and is capable of inducing immune response in
     mammal without need for adjuvant, useful as anti-tumor vaccine component.

L3   ANSWER 4 OF 7  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
TI   Use of a polypeptide self-antigen as a tumor-specific vaccine.
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L3 ANSWER 5 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.

L3 ANSWER 6 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor.

L3 ANSWER 7 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Novel polypeptide vaccine produced in plants, useful for inducing an immune response to a self-antigen on the surface of certain tumor cells.

=> d ibib abs l3 1-5,7

L3 ANSWER 1 OF 7 MEDLINE on STN
ACCESSION NUMBER: 1998263285 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9600894
TITLE: Optimizing the stability of single-chain proteins by linker length and composition mutagenesis.
AUTHOR: Robinson C R; Sauer R T
CORPORATE SOURCE: Department of Biology, Massachusetts Institute of Technology, Cambridge MA 02139, USA.
CONTRACT NUMBER: AI-15706 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 May 26) 95 (11) 5929-34. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980622

AB Linker length and composition were varied in libraries of single-chain Arc repressor, resulting in proteins with effective concentrations ranging over six orders of magnitude (10 microM-10 M). Linkers of 11 residues or more were required for biological activity. Equilibrium stability varied substantially with linker length, reaching a maximum for glycine-rich linkers containing 19 residues. The effects of linker length on equilibrium stability arise from significant and sometimes opposing changes in folding and unfolding kinetics. By fixing the **linker length** at 19 residues and **varying** the ratio of Ala/Gly or Ser/Gly in a 16-residue-randomized region, the effects of linker flexibility were examined. In these libraries, composition rather than sequence appears to determine stability. Maximum stability in the Ala/Gly **library** was observed for a protein containing 11 alanines and five glycines in the randomized region of the linker. In the Ser/Gly **library**, the most stable protein had seven serines and nine glycines in this region. Analysis of folding and unfolding rates suggests that alanine acts largely by accelerating folding, whereas serine acts predominantly to slow unfolding. These results demonstrate an important role for linker design in determining the stability and folding kinetics of single-chain proteins and suggest strategies for optimizing these parameters.

L3 ANSWER 2 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94260014 EMBASE

DOCUMENT NUMBER: 1994260014
TITLE: Genetic analysis of the nsP3 region of Sindbis virus: Evidence for roles in minus-strand and subgenomic RNA synthesis.
AUTHOR: LaStarza M.W.; Lemm J.A.; Rice C.M.
CORPORATE SOURCE: Department of Molecular Microbiology, Washington Univ. School of Medicine, Box 8230, 660 S. Euclid Ave.,St. Louis, MO 63110-1093, United States
SOURCE: Journal of Virology, (1994) 68/9 (5781-5791).
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Sindbis virus nonstructural polyproteins and their cleavage products are believed to be essential components of viral RNA replication and transcription complexes. Although numerous studies have investigated the effect of mutations in nsP1-, nsP2-, and nsP4-coding regions on Sindbis virus-specific RNA synthesis, relatively little is known about the function of the region encoding nsP3. nsP3 is a phosphoprotein comprising two regions: an N-terminal portion which is highly conserved among alphaviruses and a C- terminal portion which is not conserved, **varying** both in sequence and in **length**. We have constructed a **library** of random **linker** insertion mutations in the nsP3-coding region and characterized selected viable mutants. Initially, 126 mutants containing insertions in the conserved region and 23 with insertions in the nonconserved region were screened for temperature-sensitive (ts) plaque formation or for significant differences in plaque morphology. All nonconserved-region mutants were similar to the parental virus, whereas 13 of those in the conserved region were either ts or exhibited altered plaque phenotypes. Ten of these 13 mutants were ts for plaque formation as well as RNA accumulation at 40°C. Highly ts mutants CR3.36 and CR3.39 were defective in their ability to synthesize minus-strand RNAs at the nonpermissive temperature. The CR3.36 and CR3.39 insertion mutations localized to different regions near nsP3 residues 58 and 226, respectively. CR3.39 was able to complement ts mutants from Sindbis virus complementation groups A, B, F, and G. Another mutant isolated from the **library**, CR3.34, while not ts for plaque formation or RNA synthesis, formed smaller plaques and was defective in subgenomic RNA synthesis at all temperatures examined. These results suggest a role for nsP3 or nsP3-containing polyproteins in the synthesis of viral minus-strand and subgenomic RNAs.

L3 ANSWER 3 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-492153 [46] WPIDS
CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]
DOC. NO. NON-CPI: N2003-390915
DOC. NO. CPI: C2003-131636
TITLE: Novel polypeptide antigen which includes epitope overexpressed by tumor cells e.g. B-cell lymphoma, and is capable of inducing immune response in mammal without need for adjuvant, useful as anti-tumor vaccine component.
DERWENT CLASS: B04 D16 P13
INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H; TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I) REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2003039659 | A1 | 20030227 | (200346)* | | 48 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 2003039659 | A1 Provisional | US 1999-155979P | 19990924 |
| | Div ex | US 2000-522900 | 20000310 |
| | | US 2002-67892 | 20020208 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US 2000-522900 20000310; US 2002-67892 20020208

AN 2003-492153 [46] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]

AB US2003039659 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen (I) useful as tumor- specific vaccine in subject with a tumor, including an epitope or epitope unique to, or overexpressed by, cells of the tumor, is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from tumor of subject, and is capable of inducing an immune response in a mammal without a need for adjuvant or other immunostimulatory materials, is new.

DETAILED DESCRIPTION - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new. The polypeptide:

(a) includes an epitope or epitope unique to, or overexpressed by, cells of the tumor, thus distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folder from, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form; or

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of variable heavy (VH) and variable light (VL) domains and are linked by an amino acid linker, comprising:

(a) joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a linker to produce a first nucleic acid construct;

(b) joining the nucleic acid encoding a second part of the linker to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct;

(c) incorporating the first and second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the linker, transfecting a plant with the vector so that the plant transiently produces the polypeptide; and

(d) recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific immune response, e.g. a idiotype-specific anti-lymphoma immune response, comprising (I) produced transiently in a plant, and which is a 2-domain scFv antibody that includes part of VH and VL domains and are linked by an amino acid linker, and a carrier or excipient;

(3) a vaccine composition (IV) useful for inducing a polyclonal immune response to an idiotype in a mouse comprising (II) and a carrier or excipient; and

(4) producing (I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inducer of protective anti-tumor immune response (cellular, humoral or both) in a mammal; Vaccine.

An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ) using mRNA from the lymphoma cells to make cDNA which is PCR amplified using appropriate primers to amplify the VH and VL coding sequences. This DNA was expressed in a Nicotiana benthamiana plant by cloning into modified tobamoviral vector using the random linker **library** approach. The scFv corresponding to JJ's lymphoma surface Ig idiotype was obtained from the plants and formulated into a vaccine. The vaccine was administered by successive SC injections of 0.5 mg of the antigen. JJ's response was evaluated by laboratory tests and clinical observation. The following results were obtained. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponds to the idiotypic lymphoma surface Ig). JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H-thymidine incorporation and by secretion of interferon- gamma . JJ's peripheral blood mononuclear cells also produce tumor necrosis factor (TNF)- alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma.

USE - (I) is useful for inducing an immune response, preferably a protective anti-tumor immune response in a mammal, preferably human. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject (preferably human) or a subject who had a tumor and was treated so that no tumor is clinically radiographically evident. (III) comprises the polypeptide in unit dosage form in aqueous solution at a concentration of 0.1-10 mg/ml. The vaccines are preferably useful for inducing immune antibody response against B-cell lymphoma. (All claimed.)

ADVANTAGE - The polypeptide is produced without the need for denaturation or renaturation. (I) is rapidly produced in plants by transient viral expression. Plant samples expressing the desired protein can be positively identified by both enzyme linked immunosorbent assay (ELISA) and Western blotting 4 weeks after molecular cloning. Thus, (I) is expressed rapidly and easily in plants.

Dwg.0/5

L3 ANSWER 4 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-492106 [46] WPIDS

CROSS REFERENCE: 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492153 [46]

DOC. NO. NON-CPI: N2003-390889

DOC. NO. CPI: C2003-131600

TITLE: Use of a polypeptide self-antigen as a tumor-specific vaccine.

DERWENT CLASS: B04 D16 P13

INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H; TUSE, D

PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I) REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2003035807 | A1 | 20030220 | (200346)* | | 47 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 2003035807 | A1 Provisional | US 1999-155979P | 19990924 |
| | Div ex | US 2000-522900 | 20000310 |
| | | US 2002-67790 | 20020208 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US 2000-522900 20000310; US 2002-67790 20020208

AN 2003-492106 [46] WPIDS

CR 2001-596903 [67]; 2003-456551 [43]; 2003-456552 [43]; 2003-492153 [46]

AB US2003035807 A UPAB: 20030719

NOVELTY - A polypeptide self-antigen useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor and is encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - The polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, for distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(d) is capable of inducing an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitopes.

INDEPENDENT CLAIMS are also included for:

(1) an individual-specific immunogenic product comprising the polypeptide;

(2) a vaccine composition;

(3) inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident; and

(4) producing the polypeptide.

ACTIVITY - Cytostatic.

No suitable data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The polypeptide self antigen is useful for treating or preventing tumor.

Dwg.0/5

L3 ANSWER 5 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2003-456552 [43] WPIDS |
| CROSS REFERENCE: | 2001-596903 [67]; 2003-456551 [43]; 2003-492106 [46]; 2003-492153 [46] |
| DOC. NO. CPI: | C2003-121384 |
| TITLE: | Novel polypeptide self-antigen useful as tumor-specific vaccine in mammals, is produced in plants and mimics one or more epitopes of antigen uniquely expressed by cells of tumor. |
| DERWENT CLASS: | B04 D16 |

INVENTOR(S): LINDBO, J A; MCCORMICK, A A; REINL, S J; TURPEN, T H; TUSE, D
PATENT ASSIGNEE(S): (LIND-I) LINDBO J A; (MCCO-I) MCCORMICK A A; (REIN-I) REINL S J; (TURP-I) TURPEN T H; (TUSE-I) TUSE D
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2003044420 | A1 | 20030306 | (200343)* | | 47 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 2003044420 | A1 Provisional | US 1999-155979P | 19990924 |
| | Div ex | US 2000-522900 | 20000310 |
| | | US 2002-67893 | 20020208 |

PRIORITY APPLN. INFO: US 1999-155979P 19990924; US 2000-522900 20000310; US 2002-67893 20020208
AN 2003-456552 [43] WPIDS
CR 2001-596903 [67]; 2003-456551 [43]; 2003-492106 [46]; 2003-492153 [46]
AB US2003044420 A UPAB: 20030928
NOVELTY - A polypeptide self-antigen (I) useful as a tumor- specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded by a nucleic acid (NA) in the cells of the tumor, including an epitope to, or overexpressed by tumor cells; produced in a cell or organism that has been transfected with NA and in a correctly folded form; and capable of inducing an immune response in a mammal, is new.

DETAILED DESCRIPTION - (I) is useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, which polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of the tumor, so distinguishing the tumor from all other tumors of the same or different histological type, in the subject or in another member of the subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject;

(c) is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form;

(d) is capable of including an immune response in a mammal, including the subject, without a need for adjuvant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated immune response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I), produced by a method which involves joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a linker to produce a first nucleic acid construct, joining the nucleic acid encoding a second part of the linker to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct, incorporating the first and the second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the linker, transfecting a plant with the vector so that the plant transiently produces the polypeptide, and recovering the polypeptide as a soluble, correctly-folded protein;

(2) a vaccine composition (III) useful for inducing a tumor specific

immune response, idiotype-specific anti-lymphoma immune response, and polyclonal immune response to an idiotype of a surface immunoglobulin or to an idiotype in a mouse, comprising (I), and a pharmaceutical carrier or excipient; and

(3) production of (I).

ACTIVITY - Anti-tumor; Cytostatic.

MECHANISM OF ACTION - Vaccine (claimed). Treatment of lymphoma patient with the scFv polypeptide vaccine was demonstrated as follows. An idiotype-bearing scFv was produced from lymphoma cells of a human subject (designated JJ). JJ was subjected to immunization, and JJ's response was evaluated by laboratory tests and clinical observation. JJ's serum contained antibodies specific for the vaccine immunogen and reactive with a monoclonal Ig (that corresponded to the idiotypic lymphoma surface Ig). The antibodies were detected in an enzyme linked immunosorbent assay (ELISA) and by fluorescence activated cell sorter (FACS) analysis using cryopreserved lymphoma cells from JJ. JJ's peripheral blood T lymphocytes responded significantly in vitro to the vaccine polypeptide (or to the lymphoma cells as stimulators) by proliferation, measured as 3H- thymidine incorporation and by secretion of interferon- gamma . JJ's peripheral blood mononuclear cells also produced TNF alpha in response to these stimuli. JJ's clinical response was characterized by radiographic evidence of lack of tumor progression and gradual disappearance of the lymphoma. No radiographic or other clinical signs of relapse were evident over one year of observation.

USE - (I) is useful as a tumor-specific vaccine, especially a B-cell lymphoma-specific vaccine. (III) is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject, preferably human or a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, where the tumor is B-cell lymphoma (claimed). Dwg.0/5

L3 ANSWER 7 OF 7 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-596903 [67] WPIDS

CROSS REFERENCE: 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]

DOC. NO. CPI: C2001-176650

TITLE: Novel polypeptide vaccine produced in plants, useful for inducing an immune response to a self-antigen on the surface of certain tumor cells.

DERWENT CLASS: B04 D16

INVENTOR(S): REINL, S J; TURPEN, T H; LINDBO, J A; MCCORMICK, A A; TUSE, D

PATENT ASSIGNEE(S): (LARG-N) LARGE SCALE BIOLOGY CORP; (MCCO-I) MCCORMICK A A; (TUSE-I) TUSE D

COUNTRY COUNT: 95

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2001068682 | A1 | 20010920 | (200167)* | EN | 89 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2001012019 | A | 20010924 | (200208) | | |
| EP 1263779 | A1 | 20021211 | (200301) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | | | |
| JP 2003527399 | W | 20030916 | (200362) | | 117 |
| ZA 2002006798 | A | 20031126 | (200402) | | 94 |

EP 1263779 B1 20041215 (200482) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 60016806 E 20050120 (200510)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2001068682 | A1 | WO 2000-US28362 | 20001013 |
| AU 2001012019 | A | AU 2001-12019 | 20001013 |
| EP 1263779 | A1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| JP 2003527399 | W | WO 2000-US28362 | 20001013 |
| | | JP 2001-567772 | 20001013 |
| ZA 2002006798 | A | ZA 2002-6798 | 20020826 |
| EP 1263779 | B1 | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |
| DE 60016806 | E | DE 2000-00016806 | 20001013 |
| | | EP 2000-973516 | 20001013 |
| | | WO 2000-US28362 | 20001013 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2001012019 | A | Based on | WO 2001068682 |
| EP 1263779 | A1 | Based on | WO 2001068682 |
| JP 2003527399 | W | Based on | WO 2001068682 |
| EP 1263779 | B1 | Based on | WO 2001068682 |
| DE 60016806 | E | Based on | EP 1263779 |
| | | Based on | WO 2001068682 |

PRIORITY APPLN. INFO: US 2000-522900 20000310
AN 2001-596903 [67] WPIDS
CR 2003-456551 [43]; 2003-456552 [43]; 2003-492106 [46]; 2003-492153 [46]
AB WO 200168682 A UPAB: 20050211
NOVELTY - A polypeptide self-antigen (I) useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of the tumor, is new.

DETAILED DESCRIPTION - (I) includes an epitope or epitopes unique to, or over expressed by, cells of the tumor, thereby distinguishing the tumor from all other tumors of the same or different histological type, or in the subject or in another member of the subject's species. (I) is produced in a cell or organism that has been transformed or transfected with the nucleic acid derived from the tumor of the subject, is obtainable from the cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics the epitope or epitopes in their native form. (I) is capable of inducing an immune response in a mammal, including the subject, without a need for adjvuant or other immunostimulatory materials, so that administration of the polypeptide results in an antibody or cell-mediated response to the epitope or epitopes.

INDEPENDENT CLAIMS are also included for the following:

(1) an individual-specific immunogenic product (II) comprising (I);

(2) a vaccine composition (VC) useful for inducing a tumor-specific immune response, idiotype-specific anti-lymphoma immune response, a polyclonal immune response to at least one idiotype of a surface immunoglobulin or a polyclonal immune response to an idiotype in a mouse, comprising (I); and

(3) producing (I).

ACTIVITY - Cytostatic; immunostimulator. The idiotype-bearing self antigen was administered by successive subcutaneous injection of 0.5 mg of

the antigen and ISAF-1 adjuvant to humans with low grade B-cell lymphoma. The patients were given additional injections once a month for 5 months and booster doses were given annually. The results indicated that at least 6 of the 20 patients showed both immunological and clinical, including radiographic, signs of therapeutic success. The sera had significant titers of antibodies specific for the idiotype of their lymphoma cells and ScFV polypeptide used for immunization. Clinically, no signs of tumor progression and a statistically significant prolonged disease free interval after vaccination compared to historical controls, were observed. PCR (polymerase chain reaction) analysis of lymphocyte DNA across bcl-2/Igh, a molecular marker of human lymphoma, further confirmed the successful treatment of the lymphoma.

MECHANISM OF ACTION - Polyclonal anti-idiotypic antibody response inducer; cell-mediated immune response inducer (claimed).

USE - VC is useful for inducing a tumor-specific immune antibody response in a tumor-bearing subject or a subject who had a tumor e.g. B-cell lymphoma, and was treated so that no tumor is clinically or radiographically evident. (I) is useful for inducing a protective antitumor immune response (claimed).

ADVANTAGE - (I) can be produced at high levels, easy to purify and can be appropriately folded to mimic the conformation of the native epitopes displayed at the tumor cell surface.

Dwg.0/5

=> FIL STNGUIDE

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| FULL ESTIMATED COST | 36.21 | 36.84 |

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=> fil medline biosis caplus embase wpids

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|---|---|---|
| FULL ESTIMATED COST | 0.66 | 37.50 |

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:55:38 ON 24 FEB 2005
L1 87 (VARY OR VARYING) (10A) (SIZE OR LENGTH) (10A) LINKER
L2 39 DUP REM L1 (48 DUPLICATES REMOVED)
L3 7 LIBRARY AND L2

FILE 'STNGUIDE' ENTERED AT 12:58:17 ON 24 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 13:04:59 ON 24 FEB 2005

=> l2 not l3
L4 32 L2 NOT L3

=> t ti l4 1-32

L4 ANSWER 1 OF 32 MEDLINE on STN
TI Antigen binding and stability properties of non-covalently linked anti-CD22 single-chain Fv dimers.

L4 ANSWER 2 OF 32 MEDLINE on STN
TI Micromixing with linked chains of paramagnetic particles.

L4 ANSWER 3 OF 32 MEDLINE on STN
TI Conjugation of a hairpin pyrrole-imidazole polyamide to a quinone methide for control of DNA cross-linking.

L4 ANSWER 4 OF 32 MEDLINE on STN
TI Design and synthesis of C-8 linked pyrrolobenzodiazepine-naphthalimide hybrids as anti-tumour agents.

L4 ANSWER 5 OF 32 MEDLINE on STN
TI Poly(ethylene glycol) (PEG) conjugated arginine deiminase: effects of PEG formulations on its pharmacological properties.

L4 ANSWER 6 OF 32 MEDLINE on STN
TI Molecular dynamics simulations of calcium-free calmodulin in solution.

L4 ANSWER 7 OF 32 MEDLINE on STN
TI UP element-dependent transcription at the Escherichia coli rrnB P1 promoter: positional requirements and role of the RNA polymerase alpha subunit linker.

L4 ANSWER 8 OF 32 MEDLINE on STN
TI Simple repetitive sequences in the genome: structure and functional significance.

L4 ANSWER 9 OF 32 MEDLINE on STN
TI Fluorescence energy-transfer cyanine heterodimers with high affinity for double-stranded DNA. I. Synthesis and spectroscopic properties.

L4 ANSWER 10 OF 32 MEDLINE on STN
TI A chromatin folding model that incorporates linker variability generates fibers resembling the native structures.

L4 ANSWER 11 OF 32 MEDLINE on STN
TI Netropsin and bis-netropsin analogs as inhibitors of the catalytic activity of mammalian DNA topoisomerase II and topoisomerase cleavable complexes.

L4 ANSWER 12 OF 32 MEDLINE on STN

TI Anomalously slow electrophoretic mobilities of DNA restriction fragments in polyacrylamide gels are not eliminated by increasing the gel pore size.

L4 ANSWER 13 OF 32 MEDLINE on STN
TI DNA-directed alkylating agents. 3. Structure-activity relationships for acridine-linked aniline mustards: consequences of **varying** the **length** of the **linker** chain.

L4 ANSWER 14 OF 32 MEDLINE on STN
TI Binding of N-acetylgalactosamine-specific lectins to spin-labeled galactosamine derivatives.

L4 ANSWER 15 OF 32 MEDLINE on STN
TI Higher order structure of chromatin: evidence from photochemically detected linear dichroism.

L4 ANSWER 16 OF 32 MEDLINE on STN
TI Potential antitumor agents. 44. Synthesis and antitumor activity of new classes of diacridines: importance of linker chain rigidity for DNA binding kinetics and biological activity.

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Investigation of Aromatic Stacking Interactions through an Azobenzene Photoswitch

L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of dibenzo-16-crown-5 compounds with pendant ester and ether groups

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Genetically encoded fusion protein fluorescent reporters of kinase, methyltransferase, and acetyltransferase activities in cells and tissues

L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Atomistic Simulations of End-Linked Poly(dimethylsiloxane) Networks: Structure and Relaxation

L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Stabilization of therapeutic RNA prepared by transcription in situ by formation of a double helix involving the 5'- and 3'-terminal regions

L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor activity and therapy

L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Preparation and evaluation of unilamellar liposomes incorporating boron-containing derivatives of cholesterol

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Methods of attaching unprotected oligonucleotides to DNA-binding, fluorescent, or reactive ligands for synthesis of antisense or gene-directed agents and probes

L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Synthesis of more rigid consolidated ligands for the dual Src homology domain SH(32) of Abelson: Strategies to achieve higher affinities

L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Controlled porosity in hydrogels using micellar surfactant templates analysis using gel permeation chromatography and atomic force microscopy.

L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Design and efficient synthesis of novel DNA interstrand crosslinking agents. C(2)-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Application of bifunctional poly(ethylene glycol) derivatives in the activation of cellulose supports

L4 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Pore-size distributions of cationic 2-hydroxyethyl methacrylate (HEMA) hydrogels

L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
TI Pore-**Size** Distributions of Cationic Polyacrylamide Hydrogels **Varying** in Initial Monomer Concentration and Cross-**Linker** /Monomer Ratio

L4 ANSWER 31 OF 32 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Preparation and properties of starch-based colloidal microgels.

L4 ANSWER 32 OF 32 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Spatial distance determination method for polymer molecule or complex, e.g. biopolymers, uses transformation via mixtures of cross-linker molecules.

=> d ibib abs l4 1,8,10,13,16,19,22,24,25

L4 ANSWER 1 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2004616964 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15589829
TITLE: Antigen binding and stability properties of non-covalently linked anti-CD22 single-chain Fv dimers.
AUTHOR: Arndt Michaela A E; Krauss Jurgen; Rybak Susanna M
CORPORATE SOURCE: SAIC, National Cancer Institute at Frederick, Frederick, MD 21702, USA.. michaela.arndt@medizin.uni-essen.de
CONTRACT NUMBER: N01-CO-12400 (NCI)
SOURCE: FEBS letters, (2004 Dec 17) 578 (3) 257-61.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050129
Entered Medline: 20050128
AB By **varying linker length** and domain orientation three multivalent derivatives of a monovalent anti-CD22 single-chain fragment variable (scFv) antibody were generated. Shortening the linker of the V(H)-V(L) oriented scFv to 5 or 0 residues resulted in the formation of diabodies or a mixture of tetramers and trimers, respectively. Unexpectedly, a V(L)-0-V(H) scFv assembled to homogenous dimers, remained substantially more stable than the V(H)-5-V(L) diabody when incubated in human serum at 37 degrees C, and retained its dimeric state when concentrated up to 4 mg/ml. These properties suggest the V(L)-0-V(H) scFv could become an attractive vehicle for the selective delivery of multiple effector molecules to CD22(+) tumor cells.

L4 ANSWER 8 OF 32 MEDLINE on STN
ACCESSION NUMBER: 96126930 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8582360
TITLE: Simple repetitive sequences in the genome: structure and functional significance.
AUTHOR: Brahmachari S K; Meera G; Sarkar P S; Balagurumoorthy P; Tripathi J; Raghavan S; Shaligram U; Pataskar S
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India.
SOURCE: Electrophoresis, (1995 Sep) 16 (9) 1705-14. Ref: 92
Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960327
Last Updated on STN: 19960327
Entered Medline: 19960321

AB The current explosion of DNA sequence information has generated increasing evidence for the claim that noncoding repetitive DNA sequences present within and around different genes could play an important role in genetic control processes, although the precise role and mechanism by which these sequences function are poorly understood. Several of the simple repetitive sequences which occur in a large number of loci throughout the human and other eukaryotic genomes satisfy the sequence criteria for forming non-B DNA structures in vitro. We have summarized some of the features of three different types of simple repeats that highlight the importance of repetitive DNA in the control of gene expression and chromatin organization. (i) (TG/CA)n repeats are widespread and conserved in many loci. These sequences are associated with nucleosomes of **varying linker length** and may play a role in chromatin organization. These Z-potential sequences can help absorb superhelical stress during transcription and aid in recombination. (ii) Human telomeric repeat (TTAGGG)n adopts a novel quadruplex structure and exhibits unusual chromatin organization. This unusual structural motif could explain chromosome pairing and stability. (iii) Intragenic amplification of (CTG)n/(CAG)n trinucleotide repeat, which is now known to be associated with several genetic disorders, could down-regulate gene expression in vivo. The overall implications of these findings vis-a-vis repetitive sequences in the genome are summarized.

L4 ANSWER 10 OF 32 MEDLINE on STN
ACCESSION NUMBER: 94022307 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8415647
TITLE: A chromatin folding model that incorporates linker variability generates fibers resembling the native structures.
AUTHOR: Woodcock C L; Grigoryev S A; Horowitz R A; Whitaker N
CORPORATE SOURCE: Department of Biology, University of Massachusetts, Amherst 01003.
CONTRACT NUMBER: GM43786 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Oct 1) 90 (19) 9021-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117

Entered Medline: 19931110

AB The "30-nm" chromatin fibers, as observed in eukaryotic nuclei, are considered a discrete level in a hierarchy of DNA folding. At present, there is considerable debate as to how the nucleosomes and linker DNA are organized within chromatin fibers, and a number of models have been proposed, many of which are based on helical symmetry and imply specific contacts between nucleosomes. However, when observed in nuclei or after isolation, chromatin fibers show considerable structural irregularity. In the present study, chromatin folding is considered solely in terms of the known properties of the nucleosome-linker unit, taking into account the relative rotation between consecutive nucleosomes that results from the helical twist of DNA. Model building based on this premise, and with a constant length of linker DNA between consecutive nucleosomes, results in a family of fiber- and ribbon-like structures. When the **linker length** between nucleosomes is allowed to **vary**, as occurs in nature, fibers showing the types of irregularity observed in nuclei and in isolated chromatin are created. The potential application of the model in determining the three-dimensional organization of chromatin in which nucleosome positions are known is discussed.

L4 ANSWER 13 OF 32 MEDLINE on STN
ACCESSION NUMBER: 91039148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2231599
TITLE: DNA-directed alkylating agents. 3. Structure-activity relationships for acridine-linked aniline mustards: consequences of **varying** the **length** of the **linker** chain.
AUTHOR: Valu K K; Gourdie T A; Boritzki T J; Gravatt G L; Baguley B C; Wilson W R; Wakelin L P; Woodgate P D; Denny W A
CORPORATE SOURCE: School of Medicine, Department of Pathology, University of Auckland, New Zealand.
SOURCE: Journal of medicinal chemistry, (1990 Nov) 33 (11) 3014-9. Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19970203
Entered Medline: 19901206

AB Four series of acridine-linked aniline mustards have been prepared and evaluated for in vitro cytotoxicity, in vivo antitumor activity, and DNA cross-linking ability. The anilines were attached to the DNA-intercalating acridine chromophores by link groups (-O-, -CH2-, -S-, and -SO2-) of widely varying electronic properties, providing four series of widely differing mustard reactivity where the alkyl chain linking the acridine and mustard moieties was varied from two to five carbons. Relationships were sought between chain length and biological properties. Within each series, increasing the chain length did not alter the reactivity of the alkylating moiety but did appear to position it differently on the DNA, since cross-linking ability (measured by agarose gel assay) altered with chain length, being maximal with the C4 analogue. The in vivo antitumor activities of the compounds depended to some extent on the reactivity of the mustard, with the least reactive SO2 compounds being inactive. However, DNA-targeting did appear to allow the use of less reactive mustards, since the S-linked acridine mustards showed significant activity whereas the parent S-mustard did not. Within each active series, the most active compound was the C4 homologue, suggesting some relationship between activity and extent of DNA alkylation.

L4 ANSWER 16 OF 32 MEDLINE on STN

ACCESSION NUMBER: 86062503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4067986
TITLE: Potential antitumor agents. 44. Synthesis and antitumor activity of new classes of diacridines: importance of linker chain rigidity for DNA binding kinetics and biological activity.
AUTHOR: Denny W A; Atwell G J; Baguley B C; Wakelin L P
SOURCE: Journal of medicinal chemistry, (1985 Nov) 28 (11) 1568-74. Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198512
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19851227

AB Four classes of diacridines, joined at the 9-position by **linker** chains of **varying length**, rigidity, and polarity, were evaluated for DNA-binding properties and antitumor activity. Diacridines linked by flexible chains of varying polarity show relatively fast chromophore exchange kinetics among DNA binding sites but slower dissociation rates, suggesting the potential for considerable "creeping" of the drug along the helix, and are inactive in vivo. The exchange kinetics can be slowed dramatically by inclusion of positive charges in the side chain, but the resulting polycationic drugs are inactive in vivo, possibly due to poor distribution. Diacridines linked by a rigid, polar but neutral dicarbamoylpyrazole chain retain slow exchange kinetics, have a greatly reduced potential "creep rate", and possess good in vitro potency and significant in vivo antileukemic activity.

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:430935 CAPLUS
DOCUMENT NUMBER: 141:18691
TITLE: Genetically encoded fusion protein fluorescent reporters of kinase, methyltransferase, and acetyltransferase activities in cells and tissues
INVENTOR(S): Ting, Alice Y.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004044168 | A2 | 20040527 | WO 2003-US36059 | 20031112 |
| WO 2004044168 | C1 | 20040722 | | |
| WO 2004044168 | A3 | 20041021 | | |
| W: CA, JP | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | |
| US 2004265906 | A1 | 20041230 | US 2003-634740 | 20030805 |
| PRIORITY APPLN. INFO.: | | | US 2002-425578P P | 20021112 |
| | | | US 2003-634740 A | 20030805 |

AB The invention provides fusion protein reporter mols. that can be used to monitor protein modifications (e.g., histone modifications) in living cells, and methods of using the fusion reporter mols. for diagnosing protein-modification-associated disorders (e.g. histone-modification-associated disorders). Reporters are designed by fusing, in order from N- to

C-terminus, cyan fluorescent protein (CFP), a binding domain specific for the modified histone sequence of interest, a peptide substrate corresponding to the N-terminus of histone H3 or H4, and yellow fluorescent protein (YFP). Modification of the peptide substrate by a kinase, acetyltransferase, or methyltransferase then allows it to form an intramol. complex with the binding domain, increasing fluorescence resonance energy transfer (FRET) between the two flanking fluorescent moieties. Removal of the modification by a phosphatase, deacetylase, or (if methylation is reversible) demethylase reverses the FRET change. This design is optimized empirically to maximize responsivity by interchanging the donor and acceptor or the substrate and binding domain, or by **varying** the **length** and content of interdomain spacer sequences (**linker** sequences). Gcn5-based and TAFAB-based histone acetylation reporters are emphasized. The invention also provides methods of using the fusion protein reporters to identify candidate pharmaceutical agents that effect protein modification in cells and tissues, thus permitting identification of candidate pharmaceutical agents for treatment of protein-modification-associated disorders.

L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:924005 CAPLUS
DOCUMENT NUMBER: 136:49347
TITLE: Chimeric binding agent comprising cytokine, linker and cytokine receptor and uses in modulating receptor activity and therapy
INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon
PATENT ASSIGNEE(S): Asterion Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001096565 | A2 | 20011220 | WO 2001-GB2645 | 20010618 |
| WO 2001096565 | A3 | 20020801 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1290170 | A2 | 20030312 | EP 2001-940731 | 20010618 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004503243 | T2 | 20040205 | JP 2002-510682 | 20010618 |
| US 2004071655 | A1 | 20040415 | US 2003-311473 | 20030718 |
| PRIORITY APPLN. INFO.: | | | GB 2000-14765 A | 20000616 |
| | | | GB 2001-5969 A | 20010310 |
| | | | GB 2001-6487 A | 20010316 |
| | | | WO 2001-GB2645 W | 20010618 |

AB The invention provides a binding agent comprising a first part capable of binding a ligand binding domain of a receptor linked to a second part comprising a receptor binding domain wherein said binding agent modulates the activity of the receptor. The inventors link growth hormone (GH), through its C-terminal and a linker to the N-terminus of the SD100 domain of growth hormone receptor (GHR). By **varying** the **length**

of the **linker** inventors define a mol. that has the flexibility to allow binding of GH through site 1 to full length receptor at the cell surface. The invention also relates to methods, vectors and host cells for production of said chimeric binding agent.

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:15932 CAPLUS
DOCUMENT NUMBER: 135:195439
TITLE: Methods of attaching unprotected oligonucleotides to DNA-binding, fluorescent, or reactive ligands for synthesis of antisense or gene-directed agents and probes
AUTHOR(S): Boutorine, A. S.; Grimm, G. N.; Helene, C.
CORPORATE SOURCE: Laboratory of Biophysics, National Museum of Natural History INSERM U201-CNRS UMR 8646, Paris, 75231, Fr.
SOURCE: Molecular Biology (Translation of Molekulyarnaya Biologiya (Moscow)) (2000), 34(6), 804-813
CODEN: MOLBBJ; ISSN: 0026-8933
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The article describes the optimized methods for covalent attachment of unprotected oligonucleotides to functionally important ligands through their terminal phosphate or thiophosphate, including covalent attachment of one oligonucleotide to another. A comparative description of methods is presented for selective introduction of the phosphate, thiophosphate, amino, sulfhydryl, aldehyde, carboxylic, and other groups into the terminal nucleotide using chemical and enzymic reactions both in aqueous and organic media. Depending on their chemical nature, these groups can then interact with electrophilic or nucleophilic ligands carrying aliphatic or aromatic amino groups, hydrazido, sulfhydryl, disulfide, carboxylic, hydroxyl, aldehyde, bromo- or iodoalkyl, isothiocyanate, and other functions. The available methods allow one to **vary** the **size** of the **linker** between the oligonucleotide and ligand, its hydrophobicity and stability in acidic or alkaline media. The use of the disulfide bond permits cleavage of the oligonucleotide-ligand linkage in mild conditions.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:894759 CAPLUS
DOCUMENT NUMBER: 134:252620
TITLE: Synthesis of more rigid consolidated ligands for the dual Src homology domain SH(32) of Abelson: Strategies to achieve higher affinities
AUTHOR(S): Chen, Lin; Xu, Qinghong; Cowburn, David; Barany, George
CORPORATE SOURCE: Department of Chemistry, University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 579-580. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. The desired branched consolidated ligand sequences were assembled by Fmoc solid-phase chemical on PEG-PS supports. The original consolidated ligands were modified by replacing the flexible Gly linkers

with more rigid spacers rich in alanine. Affinities of the new consolidated linkers were found to **vary** with **linker length**, but in general, they were higher than the original compds. with Gly linkers.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 37.16 | 74.66 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -2.92 | -2.92 |

FILE 'STNGUIDE' ENTERED AT 13:13:53 ON 24 FEB 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 18, 2005 (20050218/UP).

=> D HIS

(FILE 'HOME' ENTERED AT 12:53:52 ON 24 FEB 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:55:38 ON 24 FEB 2005

L1 87 (VARY OR VARYING) (10A) (SIZE OR LENGTH) (10A) LINKER
L2 39 DUP REM L1 (48 DUPLICATES REMOVED)
L3 7 LIBRARY AND L2

FILE 'STNGUIDE' ENTERED AT 12:58:17 ON 24 FEB 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 13:04:59 ON 24 FEB 2005

L4 32 L2 NOT L3

FILE 'STNGUIDE' ENTERED AT 13:13:53 ON 24 FEB 2005

=> logoff hold

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 1.20 | 75.86 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -2.92 |

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:25:51 ON 24 FEB 2005